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09/930,715	08/14/2001	Moncef Jendoubi	266/226	1686

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EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/930,715	Applicant(s) JENDOUBI, MONCEF	
	Examiner My-Chau T. Tran	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed 7/16/02 in Paper No. 6 is acknowledged and entered. Claims 1, 4, and 7 are amended. Claims 1-13 are pending.

Oath/Declaration

2. Applicant's submission of the oath/declaration in Paper No. 7 that corrected the defect in which the full name of each inventor (family name and at least one given name together with any initial) has not been set forth and the title, "Dr.", as part of the inventor first name, is acknowledged and entered.

Drawings

3. The corrected or substitute drawings were received on 7/16/02 in Paper No. 7. These drawings are acceptable.

4. The previous rejections 35 USC 112, second paragraph, 35 USC 102(b) and 35 USC 103(a) for claims 1-13 have been withdrawn in view of applicant's amendment and argument. Upon further consideration, the following new grounds of rejection are made as follows. Therefore, this Office action is a non-final rejection.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of an antibody (polyclonal or monoclonal) in making a matrix of protein array (pg. 10, lines 15-21; pg. 13, lines 10-24; pg. 16, lines 3-6) and to conduct gene product expression profiling of a given normal or diseased tissue (pg. 6, lines 7-15; pg. 19, lines 23-27; pg. 20, lines 3-8), does not reasonably provide enablement for the scope encompassed by the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim that is to raise a monoclonal antibody to the expression product of the gene sequence.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re* Wands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

It is noted that there is a great deal of unpredictability in raising a monoclonal antibody to the expression product of the gene sequence without knowing specifically the sequence to be use for making the antibody. The method for raising a monoclonal antibody requires different method steps (i.e. different reagents) from the method of analyzing gene expression of Claim 1.

The instant specification fails to provide a specific methodological procedure for which the instant method can or is intended to be used for raising a monoclonal antibody to the expression product of the gene sequence. The specification teachings are directed to the methods for making a matrix of protein array and conducting gene product expression profiling of a given normal or diseased tissue.

The working examples in the specification are limited to the methods for making a matrix of protein array, and conducting gene product expression profiling of a given normal or diseased tissue. Such is not seen as sufficient to support the breath of the claims, wherein the scope of the claims encompasses the method of raising a monoclonal antibody to the expression product of the gene sequence. It is noted that the Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see *In re* Gardner et al. 166 USPQ 138 (CCPA 1970). Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

7. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of raising a monoclonal antibody to the expression product of the gene sequence.

The specification discloses the use of an antibody (polyclonal or monoclonal) in making a matrix of protein array (pg. 10, lines 15-21; pg. 13, lines 10-24; pg. 16, lines 3-6) and to conduct gene product expression profiling of a given normal or diseased tissue (pg. 6, lines 7-15; pg. 19, lines 23-27; pg. 20, lines 3-8). None of these meet the written description provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the method encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement

"by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the full breadth of the claim does not meet the written description provision of 35 U.S.C 112, first paragraph.

In the presence instance, the claim contains no specific sequence or method steps regarding the method of raising a monoclonal antibody to the expression product of the gene sequence. The specification does not provide sufficient written description to support the method encompassed by the claim.

8. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of determining the polynucleotide sequence of the gene sequence.

The specification discloses only the use of a matrix protein array for the analysis of gene product (pg. 6, lines 16-22; Example 3 and 4). None of this meets the written description provision of 35 U.S.C 112, first paragraph. The specification provides insufficient written description to support the method encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the full breadth of the claim does not meet the written description provision of 35 U.S.C 112, first paragraph.

In the presence instance, the claim contains no method steps regarding the method of determining the polynucleotide sequence of the gene sequence. The specification does not provide sufficient written description to support the method encompassed by the claim.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The term "gene sequence" of Claim 1 is vague and indefinite because what specific sequence is being examined? No sequence is disclosed in the specification.

b) It is unclear what is being correlated in the correlating step of Claim 1 because it is unclear what is being examined. Are the method steps result in gene expression analysis or is it the reaction between the antibody and the sample is being examine?

c) The phrase "two distinct biological conditions that may exhibit differential gene expression" in Claim 1 is indefinite because it is unclear what is being compared. Is it two different "medical" conditions being compared such as normal versus disease state? Or is it two different time points in a time course of gene product expression profiling?

d) The term "antibody" in Claim 1 is vague and indefinite because it is unclear which antibody is being used. Is "antibody" specific to gene expression product or any other antibody? Applicants are requested to clarify.

e) The method of raising a monoclonal antibody of Claim 12 is vague and indefinite because it is how it is related with the method of analyzing gene expression of Claim 1. The method of raising a monoclonal antibody would involve different method steps that have different functions and effects than the method steps for analyzing gene expression.

f) The method of determining the polynucleotide sequence of the gene sequence of Claim 13 is vague and indefinite because it is not clear how it is related with the method of analyzing gene expression of Claim 1. The method of determining the polynucleotide sequence of the gene sequence would involve different method steps that have different functions and effects than the method steps for analyzing gene expression.

11. Claim 3 recites the limitation "100 antibodies" in line 2. There is insufficient antecedent basis for this limitation in the claim because in Claim 1 the contacting step involves an antibody. And also it is not clear whether all the 100 antibodies are the same or different. Applicants are requested to clarify.

12. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: The method step of providing the type of host animal to be use for raising the antibody or the cell lines use for culturing the antibody. The method step of adding adjuvants to increase the immunological response of host animal.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

14. Claims 1-2 and 4-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Iris et al. (US Patent 6,403,309 B1).

Iris et al. discloses a method that utilizes oligonucleotide probes labeled with distinguishable and identifiable labels, (e.g. peptide tags), that are captured on addressable antibody arrays for analysis (col. 1, lines 14-18). The method can be use for the analysis of gene expression (refers to instant claim 1) using addressable antibody array (col. 14, lines 51-67). The method is used to directly monitor qualitative and quantitative gene expression levels in tissue biopsies or histological preparations that is taken from patient with suspected genetic disorder. The RNA target is extracted from the tissue sample and hybridized with the oligonucleotide probes (col. 15, lines 32-67 to col. 16, lines 1-11). The sample is then exposed to a solid phase surface, which would be an addressable antibody arrays, comprising a binding partner to the peptide label oligonucleotide probe. The solid phase surface comprises a plurality of loci, wherein each locus comprises an antibody specific to one or more of the peptides of the peptide label oligonucleotide probes (col. 6, lines 28-31; col. 22, lines 23-29). The antibodies includes

polyclonal or monoclonal (refers to instant claim 2) (col. 23, lines 33-57). The polyclonal antibodies are produce from mice or rat. The detection of a signal would indicate the present of the target RNA (col. 16, lines 12-19). Additionally, the method can be used for multiplex screening to phenotype/genotype association analysis (col. 14, lines 24-33). A target DNA sample comprises a plurality of DNA molecules derived from a population of individuals afflicted with a disorder such as cancer. A control DNA sample comprises of DNA molecules derived from a non-afflicted populations. The two populations can be screened in multiplex with a number of peptide label oligonucleotide probes, and the results compared between the two populations. The method of Iris et al. anticipated the method of the claimed invention.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1 and 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Iris et al. (US Patent 6,403,309 B1) in view of Bandaru (US Patent 6,462,187 B1).

The methods of Iris et al. are applied for the reasons discussed above.

Iris et al. differs from the claimed invention by failing to include the plurality of antibodies to be 100.

Bandaru discloses a two dimensional array having a plurality of addresses, each address of the plurality is positionally distinguishable from each other address of the plurality (col. 4, lines 35-45; col. 51, lines 37-67). Each address of the plurality can have a unique capture probe such as polypeptide, e.g. an antibody specific for the polypeptide. The plurality of addresses includes at least 10, 100, 500, 1,000, 5,000, 10,000, 50,000 addresses (col. 49, lines 14-16). The array can be use to assay gene expression in a tissue to ascertain tissue specificity of genes in the array (col. 49, lines 62-64) or to monitor expression of one or more genes in an array with respect to time for ascertaining differential expression patterns of one or more genes in normal or abnormal cells (col. 50, lines 32-45).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Iris et al. by including the plurality of antibodies to be 100 as taught by Bandaru because both Bandaru and Iris et al. teach the method of multiplex screening of gene expression (Iris et al.: col. 14, lines 24-33; Bandaru: col. 50, lines 1-7). Therefore, one would have had reasonable expectation of success of including the plurality of

antibodies to be 100 into the method of Iris because both Bandaru and Iris teach the methods of gene expression analysis.

Response to Arguments

18. Applicant's arguments with respect to claims 1-13 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

mct
October 17, 2002

PADMASHRI PONNALURI
PRIMARY EXAMINER